asserts that the tobacco mosaic virus thus has some structural and functional utility in common with the clathrin-based invention. The USPTO therefore says C2 and C3 anticipate the instant invention, a novel bio-based laser and source of regulated photons that also has utility in quantum information processing.

Contrary to all USPTO assertions, all of the above rejected claims listed in **C1, C2, and C3** relate to <u>non-naturally</u> occurring clathrin-based systems and are the result of the hand of man. The terms "purified", and "bio-engineered," and their obvious synonyms like "man-made" and "non-naturally occurring" are referenced in the instant invention specification as well appear as in the herein amended claims. E.g., in the amended claim 1, below:

> (Currently Amended): A <u>non-naturally occurring</u> laser light source <u>offering precise control over its fabrication and operation</u> comprising:
>
> a <u>man-made</u> cage, <u>up to 100 nanometers in diameter,</u> defining a <u>calculated, artificial, environment-isolating</u> cavity <u>that is bioengineered and</u> formed from a plurality of <u>artificially-induced</u> self-assembling <u>purified Clathrin</u> protein molecules,
>
> and
>
> one or more <u>man-made</u> cargo elements <u>calculatedly</u> located within the <u>man-made</u> cavity, wherein at least one of the cargo elements contains a <u>man-made</u>, <u>artificially configured</u> fluid and or ~~a~~ quantum dot,
>
> wherein the cargo element cavity and or its contained fluid internally <u>and calculatedly</u> reflects one or more <u>artificially selected</u> wavelengths of light in response <u>to one or more artificially selected</u> <u>and induced</u> <u>frequencies of</u> electromagnetic excitation,
>
> and
>
> wherein the <u>non-natural</u> laser light source, <u>by human design</u>, emits one or more photons of <u>specified frequencies</u> of light in response to ~~an~~ <u>one or more purposely induced types of stimuli,</u> ~~stimulus~~ <u>resulting in</u>

controlled lasing that is not practically utilized in naturally occurring systems, because by definition the latter do not offer the required precise control over their fabrication and operation,

and

which stimuli can further have the optional effect, by human design, of calculatedly deforming the cargo element cavity in order to tune its Q value and resonant frequency in a purposely controlled fashion.

References re non-naturally occurring appear in the instant patent specification, some of which are enumerated and highlighted below:

0014 "... According to another feature, **the proteins that form the cage can be bio-engineered using commercially-available biotechnology tools** to contain different cargo elements, which makes the invention more versatile and cost-effective than the existing art."

"**0057** Cage 106 can be naturally occurring or **biologically engineered and/or can use synthetic proteins in whole or in part.** Also, the receptor molecules 104a-104f can be naturally occurring or **biologically engineered and/or can use synthetic proteins in whole or in part** to recognize specific cargo elements 102a-102f. Likewise, the adapter molecules 108a-108f can be naturally occurring or **biologically engineered and/or can use synthetic proteins in whole or in part** to recognize and couple to particular receptor molecules 104a-104f. "

"**0082** As mentioned above, naturally in vivo occurring clathrin cages 106 assemble around membranes to form vesicles. Referring again to Figure 1, the adapter molecules 108a-108f couple clathrin proteins 106a-106f to receptor molecules 104a-104f disposed around the periphery of the vesicle 110. **According to the illustrative embodiment, the clathrin cage 106 is formed around the vesicle 110 *in vitro* using synthetic, natural, or mixed lipid monolayers or bilayers and purified receptor 104a-104f and adapter 108a-108f molecules.** For example, in one illustrative embodiment, **the clathrin cage 106 is formed by adding biologically engineered clathrin proteins 106a-106f and adapter molecules 108a-108f, such as AP-2 and**

AP180, to a PIP2-containing lipid monolayer. According to one feature of the invention, **the receptor molecules 104a-104f are <u>biologically engineered</u>** to recognize and associate with specific molecules that serve as the cargo elements 102a-102f. According to another feature, the **adapter molecules 108a-108f are <u>biologically engineered</u>** to recognize specific receptor molecules 104a-104f and couple the receptor molecules 104a-104f to the clathrin cage 106."

"**0084** Below pH 6.5, **<u>purified</u> clathrin triskelions <u>self-assemble *in vitro*</u>** into a polyhedral lattice (cages) without vesicles, but typically only form cages at physiological pH in the presence of **<u>stoichiometric quantities</u> <u>of purified</u> AP-1 or AP-2 adaptor molecules or the neuron-specific assembly proteins AP-180 and auxilin.** Recombinant hubs, formed from residues 1074–1675 of the clathrin heavy chain, are trimeric structures that reproduce the central portion of the three-legged clathrin triskelion, extending from the vertex to the bend in each leg, comprising the binding sites for clathrin light-chain subunits. Without light-chain subunits, recombinant hubs self-assemble reversibly at physiological pH, while hubs with bound light chains self-assemble below pH 6.5, similar to **<u>purified</u> clathrin. <u>Inhibition of hub assembly</u> by light-chain subunits is a <u>key to</u> <u>controlling spontaneous</u> clathrin self-assembly at physiological pH. The mean curvature of baskets (cages without vesicles) is <u>adjustable</u> by the pH level and by other environmental conditions. As can be deduced from the formation of the microcages, a clathrin network can have such a <u>pH-controlled</u> curvature, even in the absence of a membrane bilayer**. In addition, a conserved negatively charged sequence of three residues (23–25) in the clathrin light-chain subunits regulates the pH dependence of hub assembly. Also, two classes of salt bridge (high affinity and low affinity bridges) play a dominant role in driving clathrin assembly. Basket closure depends on the presence of TDD domains (terminal and distal domains). A connection between the proximal and distal domains is not required for curvature, and the TDD themselves can orient the assembling hubs in a favorable angle for polyhedron formation."

"**0086** The heat shock cognate protein, hsc70, helps to regulate the endocytosis aftermath of CCV uncoating and disassembly. In cells overexpressing ATPase-deficient

hsc70 mutants, uncoating of CCVs is inhibited in vivo. In a preferred embodiment, an over expression of **ATPase-deficient hsc70 mutants** **may be applied and hsc70 mutants** **additionally modified via** **bioengineering techniques** to inhibit both CCV and non-vesicle cage disassembly, thereby maintaining CCV and clathrin cage integrity in the invention over prolonged periods of time in vivo and in vitro."

"0092 Bovine clathrin heavy chain cDNA encoding heavy chain amino acids 1-1074 (SEQ ID NO: 1) is cloned into the pET23d vector (Novagen) between the NcoI(234) and XhoI(158) sites. Expression of the cloned sequence results in a terminal and distal domain fragments having a C-terminal polyhistidine tag. Hub fragments corresponding to amino acids 1074-1675 (SEQ ID NO: 2) are cloned into vector pET15b (Novagen) between the BamHI(319) and XhoI(324) sites. Expression of the hub fragments produces the proximal leg domain and central trimerization domain of the clathrin hub with an N-terminal polyhistidine tag. Vectors containing the heavy chain and hub domains **are expressed in *E. coli* by induction with 0.8 mM isopropyl-B-D-thiogalactopyranoside for 3 hours at 30 degrees Celsius. Expressed proteins** are **purified** from bacterial lysate in binding buffer (50 mM Tris-HCl (pH7.9), 0.5M NaCl, 5 mM imidazole) in a nickel affinity resin using the polyhistidine tag. **Proteins are eluted with 100 mM EDTA and dialyzed against 50 mM Tris-HCl (pH7.9). Hub fragments are further purified using size exclusion chromatography on a Superose 6 column (Pharmacia)."**

"0127 Using the universal quantum gate, the quantum processor 602 can perform quantum calculations. Further, because the QIP element 100 is formed using a bioengineered protein, the cage 106 is highly scalable. For example, in some illustrative embodiments, multiple cages 106 may be physically linked via molecular addends, but are not limited to such addend types. In other illustrative configurations, multiple cages 106 may be **functionally linked** via **photonic**, chemical, electromagnetic, electrical and/or quantum (non-classical) interactions, to work and cooperate locally and/or remotely.

In sum, the instant invention requires the hand of man to exist. It further has novel utility as a quantum information processing element and also has utility as a controllable

laser and source of regulated photons. In addition, the instant inventors have specified in a number of instances in the instant application specification and herein amended claims terms such as "purified", and "bio-engineered," "man-made" and "non-naturally occurring." To someone or a person who had ordinary skill in the art it is clear that the constituent components of the instant invention are fundamentally non-equivalent to the all-natural materials cited in C2 and C3, above.

Finally, perhaps the most fundamental mistake in the USPTO's reasoning comes regarding Fujime (C2) and his use of an external laser with the tobacco mosaic virus. The methodology described by Fujime is a two-component system, in which there is a separate outside laser light source that is beamed through a tobacco mosaic virus. In marked contrast, the instant invention is a *unitary* laser system. It is a single component. Coherent laser light originates from inside the clathrin protein-caged vesicle, itself. This unitary feature therefore makes the instant invention's operating characteristics and its utility distinctly different from the Fujime-described 2-part setup. Also, Fujime's laser was used to invoke and examine quasi-elastic light scattering from solutions of molecules. Thus, Fujime's laser-virus apparatus intentionally provokes light scattering; just the opposite effect of the instant invention, which intentionally produces coherent light.

On the other hand, Namba et al (C3) do not utilize lasers. Instead, Namba employs X-ray diffraction to elucidate the structure of the tobacco mosaic virus. But quite confusingly, when discussing Namba as the reason for rejecting claims in the instant invention, the USPTO says... "The virus blocks the light radiation in a way to cause the virus to affect radiation using its cage and vesicle. The virus is interpreted as a framework of cages self assembling to form a light source. The laser is a stimulus external to the cage that to which the virus, its cavity, and its cage responds."

Strictly per the cited Namba reference, what the USPTO states is impossible, as Namba is using X-ray diffraction from oriented gels, not laser generated photons. But if the USPTO is stating that Namba's tobacco virus setup could so respond if he were to

use lasers instead of X-rays, then the USPTO's line of reasoning falls into the realm of pure conjecture with no basis in science or fact.

D.1. Re the following USPTO rejections:

I. Per 35 U.S.C.101 of Claims 1-42, 44, 47-52, 54-55, 58-59, 62-64, and 66-68 "....because the claimed invention is not supported by either a specific asserted utility or a well established utility....it is unclear how someone skilled in the art would use a laser light source or method of making a laser light source for the purpose of solving a quantum mechanics or any mathematical calculation.", and,

II. Per 35 U.S.C.101 of Claims 1-42, 44, 47-52, 54-55, 58-59, 62-64, and 66-68, because Lee, et al "shows usage of quantum dots in viruses but does not show how such particles can be used in quantum mecahnical (sic) calculations.", and,

III. Per 35 U.S.C.112, first paragraph, of claims 1-42, 44, 47-52, 54-55, 58-59, 62 64, and 66-68, because, "...Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention."

Firstly, re item D.I., in the instant application specification, it specifically asserts: "**0070** In one illustrative embodiment, highly controllable ARC nanolasers, droplet based and/or photonic-based, are a regulated source of photons for use in quantum computing and quantum cryptography."

Secondly, re D.II, there is some confusion in the argument for claims rejection by the USPTO. In the present instance, the USPTO says that Lee, et al [Science, volume 296, May 3, 2002, pages 892-896] does <u>not</u> show how photon-emitting particles like quantum dots can be used in quantum mechanical calculations, i.e., they are not programmable. But yet in its other communications to the instant inventors the USPTO apparently asserts such particles can be programmable.

Specifically, in its instant rejection of claims under 35 U.S.C.101, the USPTO states, "For example, Lee, et al shows usage of quantum dots in viruses but does not show how such particles can be used in quantum mecahnical (sic) calculations." However, and rather confusingly, in its Office Action Summary issued in response to the instant inventors' communication of April 24, 2006 regarding their other pending patents #10/661/465 and #10/661/466, the USPTO said that Lee, above, "...shows how the quantum dots are programmable by the use of a magnetic field...Thus the virus affects the magnetic radiation experienced by the quantum dots." It would appear that the USPTO has taken a contradictory stance in its claim rejections, using the same cited references.

D.2. Collectively, items D.1, D.II, and D.III are disputed by the instant inventors, because in truth, the instant patent specifically describes how photons can be used in quantum computing, and which is also expressed in the amended claims via the terms "resulting in controlled lasing", "calculatedly", "artificially configured", "by human design", "non-naturally occurring light source", and such. For example, in the instant patent specification it states:

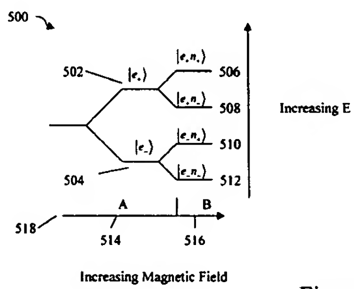

Figure 5

"**0104** By way of example, if a qubit is initially in some state representing $|0\rangle$ 504, a NOT operation can be performed by **shining a pulse of light of appropriate wavelength on a qubit** atom to force an electron to change energy levels. Thus, an electron initially in the ground state absorbs energy from the **light pulse** and is excited to the higher energy state. The wavelength of the applied light pulse must at least match the energy difference between the two energy levels separating the

logic states (i.e., between the ground state and the excited state of the nitroxide) as governed by Planck's quantization law.

$$E = \frac{hc}{\lambda}$$

where

E = energy difference between energy levels of orthogonal quantum logic states

h = Planck's constant

c = the speed of light, and

λ = wavelength of the applied pulse.

If the pulse exceeds the energy required for excitation, the extra energy is emitted as a **photon** after the electron reaches the higher energy level, i.e., $|1\rangle$."

"**0105** In a further illustrative embodiment, an applied magnetic field interacts with the electron spin, but not with the nuclear spin, i.e., in the A region 514. This configuration gives rise to two one-qubit states using spin $|0\rangle$ 502, $|1\rangle$ 504. The NOT operation in this configuration involves changing the direction of the applied magnetic field 518. In one illustrative embodiment, the electron is excited using pulses of electromagnetic radiation while maintaining its spin configuration. The source of the electromagnetic radiation may be, for example, an ordinary lamp, an LED, a time-varying magnetic field generator, **a laser**, or an electromagnetic field generator. In the illustrative embodiment, the electromagnetic source acts as a writing element."

D.3. The USPTO rejection of Claims 1-42, 44, 47-52, 54-55, 58-59, 62-64, and 66-68 under 35 U.S.C. 101 also states that "Substantial research is necessary to use light as a means of satisfying the utilities in the instant specification." Currently, there are hundreds, if not thousands of scientific papers describing utility in the area of quantum computing and using lasers and photonics. For someone or a person skilled in the art of quantum computing using optics, photons, quantum dots, and lasers, the benefit of the instant invention, a nanoscale tunable dye laser, is obvious, and its novel utility will bring significant value to the art.

Attention is drawn to eight exemplar scientific papers that were sent on Sept. 6, 2006 to the USPTO and incorporated as reference to the instant application. The eight papers' titles are:

1. A Neutral Atom Quantum Register
W. Alt,Y. Miroshnychenko, A. Rauschenbeutel and
I. Dotsenko, M. Khudaverdyan, D. Meschede, D. Schrader
Institut für Angewandte Physik der Universität Bonn, 2004

2. Coherently Manipulating Two-Qubit Quantum Information Using A Pair Of Simultaneous Laser Pulses
L. F. Wei, and F. Nori,
Europhys. Lett., 65 (1), pp. 1–6 (2004)
DOI: 10.1209/epl/i2003-10053-y, Europhysics Letters

3. Control and Measurement of Three-Qubit Entangled States
Christian F. Roos, Mark Riebe, Hartmut Haffner,
Wolfgang Hansel, Jan Benhelm, Gavin P. T. Lancaster,
Christoph Becher, Ferdinand Schmidt-Kaler, Rainer Blatt
4 June 2004 Vol 304 Science

4. Laser Addressing Of Individual Ions In A Linear Ion Trap
H. C. Nagerl, D. Leibfried, H. Rohde, G. Thalhammer, J. Eschner, F. Schmidt-Kaler, and R. Blatt
Physical Review A Volume 60, Number 1 July 1999

5. Perfect Quantum Error Correction Coding In 24 Laser Pulses
Samuel L. Braunstein
John A. Smolin (August 28, 2006)
arXiv:quant-ph/9604036 v2 22 Oct 1996

6. Quantum Computation with Ultrafast Laser Pulse Shaping
Debabrata Goswami
Resonance, June 2005

7. Speed Optimized Two-Qubit Gates with Laser Coherent Control Techniques for Ion Trap Quantum Computing
J. J. Garcıa-Ripoll, P. Zoller, and J. I. Cirac
Volume 91, Number 15, Physical Review Letters, 10 October 2003

8. Weak Nonlinearities: A New Route To Optical Quantum Computation
W J Munro, K Nemoto and T P Spiller
New Journal of Physics 7 (2005) 137, 27 May 2005

D.4. Re D.I-D.III, additional references to optics, quantum dots, regulated photons, and their relevance to quantum computing may also include the following, and are herein listed on a separate document as references to the instant application specification:

- Alivisatos, AP, Semiconductor Clusters, Nanocrystals, and Quantum Dots, Science, pp. 933-937, 1996
- Ando, T. et al. Mesoscopic Physics and Electronics (Springer, Berlin, 1998)
- Artemyev, M. V. Woggon, Quantum Dots In Photonic Dots, Applied Physics Letters, 2000
- Brown, K.R., D. A. Lidar, and K. B. Whaley, Quantum computing with quantum dots on quantum linear supports, Physical Review A, Volume 65, 2001
- Debray, P. et al. Ballistic Electron Transport In Stubbed Quantum Waveguides: Experiment And Theory. Phys. Rev. B 61, 10950±10958 (2000).
- Entanglement In Quantum Dots Via Photon Exchange, arXiv: quant ph/9906025 v1 8 Jun 1999
- Gaponenko, S. V., Optical Properties of Semiconductor Nanocrystals, Cambridge University Press, Cambridge, 1998
- Harneit, W., M. Waiblinger, K. Lips, C. Meyer, A. Weidinger, and J. Twamley in Proceedings of the IQC'01 (Sydney, Australia, 16-19th January 2001), edited by R. G. Clark (Rinton Press, 2001)
- Hill, S. C., and R. E. Benner, Optical Effects Associated with Small Particles, P. W. Barber and R. K. Chang, Eds. (World Scientific, Singapore 1988).
- Imamoglu, A., P. Petroff, E Hu, et al, A Quantum Dot Single-Photon Turnstile Device, Science, Dec. 2000
- Knill, LaFlamme, Milburn, Efficient Linear Optics Quantum Computation, Nature 409, 46, 2001)
- Michler, P., A. Imamo, M. D. Mason, P. J. Carson, G. F. Strouse, S. K. Buratto, Quantum Correlation Among Photons From a Single Quantum Dot at Room Temperature, Nature, August 2000
- Murray, CB, Norris, DJ, Bawendi, MG, Synthesis And Characterization Of Nearly Monodisperse CDE (E = S, SE, TE) Semiconductor Nanocrystallites, Journal Of The American Chemical Society, pp. 8706-8715, 1993
- Ralph, T.C., A. G. White, W. J. Munro, and G. J. Milburn, Simple scheme for efficient linear optics quantum gates, Physical Review A, Volume 65, December 2001
- Report of the NSF Workshop, Quantum Information Science, An Emerging Field of Interdisciplinary Research and Education in Science and Engineering, October 28-29, 1999 Arlington, Virginia
- Santori, Fattal, Vuckovic´, Solomon; Letters to Nature, 2002; Yamamoto Quantum Entanglement Project, ICORP, JST, E. L. Ginzton Laboratory, Stanford University). Woggon, U., Optical Properties of Semiconductor Quantum Dots, Springer, Berlin, 1996